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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF
SEDRANI ET AL.
APPLICATION NO: 09/585,743
FILED: JUNE 2, 2000
FOR: RAPAMYCIN ASSAY

Art Unit: 1641
Examiner: M. Ceperley

Assistant Commissioner for Patents
Washington, D.C. 20231

BRIEF ON APPEAL

Sir:

This appeal is lodged in response to a Final Rejection dated November 15, 2002, finally rejecting claims 28-39. Applicants request reconsideration of the rejections and reversal of the Final Rejection.

1. Real Party In Interest:

The real party in interest is Novartis AG.

2. Related Appeals and Interferences:

None.

3. Status of Claims:

Claims 28-39 (Appendix I) are pending. All are under Final Rejection and are now on appeal.

4. Status of the Amendments:

All the original claims 1-14 and intermediate claims 15-27 have been canceled. Claims 28-39 were added by amendment dated September 6, 2002.

5. Summary of the Invention:

The invention is directed to monoclonal antibodies which recognize two specific rapamycins and to an immunoassay kit which comprises said monoclonal antibodies.

The invention is also directed to hybridoma cell line which produces said monoclonal antibodies.

6. Issues:

1. Status of a provisional double-patenting rejection.

2. Whether the invention is enabled.

7. Grouping of the Appealed Claims:

The claims on appeal may be grouped as: 1) claims 28-30, 32-37, and 39; 2) claim 31; and 3) claim 38. The claims do not all stand or fall together.

8. Arguments:

1. Rejection under 35 USC 101

The claims are provisionally rejected under 35 USC 101 for double patenting over pending application 09/933,104, filed August 20, 2001. The present application was filed almost nineteen months before application 09/933,104. A first Office Action has not yet been received in said application. The provisional rejection should be withdrawn in the present application when the application is otherwise allowable and made in said second application when it is taken up for examination. (MPEP 804I.B."*... the examiner should then withdraw that rejection and permit the application to issue as a patent, thereby converting the "provisional" double patenting rejection in the other application(s) into a double patenting rejection at the time the one application issues as a patent.*")

2. Rejection under 35 USC 112

a) Group 1), claims 28-30, 32-37, and 39.

The claims are rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. In the Final Rejection, the Examiner has referred back to the reasons for rejection stated in the Office Action of June 3, 2002, wherein the basis for rejection is that the use of **any** (Examiner's

emphasis) rapamycin-carrier conjugate is not reasonably enabled. The Examiner specifically noted that "enablement is clearly present ...using specific ... rapamycin derivatives." This confirms the exemplification in the specification of antibodies produced from rapamycin and 40-O-alkylated rapamycin; i.e., the same antibodies which are being claimed. The procedure is described from the starting rapamycin, through the linkages to form immunogenic conjugates, and to the selection of hybridomas selected for the production of high-affinity monoclonal antibodies. Nothing more is necessary to enable one of ordinary skill in the art to reproduce the invention.

The Examiner states that the present claims are of the same scope as those which were previously rejected (in the Office Action of June 3, 2002). This is incorrect. The former claims, which were also rejected for lack of enablement, were directed to antibodies which recognize "a rapamycin". The present claims are of a much narrower scope; i.e., they are directed to antibodies which recognize rapamycin and 40-O-alkylated rapamycin. (*N.B.*: There is a distinction between "rapamycin" and "a rapamycin". The first term refers to a specific compound; whereas the second refers to a genus of compounds. These definitions were discussed in the Reply and Amendment dated February 27, 2002.)

The Examiner further states that: "The claims say nothing about how the monoclonal antibodies are prepared." Applicants are unaware of any statutory or regulatory requirement for a recitation in a claim of how a compound is prepared. It is not seen how failure to recite such preparation in the claim language is a deficiency under 35 USC 112.

Further, the rejection is untenable in view of the rejection (Office Action of September 27, 2001) under 35 U.S.C. 103, which the Examiner supported by stating (said Office Action at pages 6-8): *"it is considered well within the level of skill in the art ... with the expectation of conventionally using these immunogens to obtain similarly useful antibodies specific to rapamycin and its derivatives"*. Although that rejection was subsequently withdrawn by the Examiner, it is clear from the rejection that the Examiner believes that the invention can be reduced to practice by one of ordinary skill based on the state of the art. In view of this belief by the Examiner, the rejection is untenable since the enablement requirement can be met not only by what is disclosed in a patent specification but also by what is known in the art. Even if there were no exemplification of the invention in the specification, the Examiner's belief that one of ordinary skill in the art could conventionally use immunogens to obtain useful antibodies specific to rapamycin undermines the rejection based on lack of enablement.

b) Group 2), claim 31.

The claim is rejected for the same reasons as those used to reject the claims of Group 1. Applicants' arguments regarding Group 1 are repeated herein. Additionally, this is a dependent product-by-process claim for producing antibodies which recognize rapamycin and 40-O-alkylated rapamycin which recites the process steps to prepare the antibodies; i.e., the very steps which the Examiner states are missing from the claims of Group 1.

c) Group 3), claim 38.

This is a claim to a hybridoma cell line. Applicants have provided specific examples for producing antibody-producing hybridomas and the supporting literature references. There is nothing in the rejection, which is supported by arguments directed solely at the antibody claims, which is relevant to a hybridoma claim. The original hybridoma claim (13) had been rejected under 35 USC 112 for failure to recite an ATCC deposit and under 35 USC 103 for obviousness. However, those bases for rejection were not repeated following applicants' response of February 27, 2002 and are not in issue here. There is, therefore, no reason provided by the Examiner for rejection of this claim other than reasons regarding antibodies.

It is believed that the rejections under 35 USC 112 are improper and that the invention is fully enabled.

Accordingly, reconsideration of the propriety of the outstanding rejections under 35 U.S.C. 112, withdrawal of the double patenting rejection, and allowance of the claims to issue as U.S. Letters Patent is respectfully solicited.

The Commissioner is hereby authorized to charge the fee under 37 CFR 1.17(c) of $320.00 to Deposit Account No. 19-0134

Respectfully submitted,

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Encls.: Appeal Brief in triplicate with Appendix
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APPENDIX I

28. A monoclonal antibody which specifically recognizes a rapamycin, wherein the rapamycin is (i) rapamycin or (ii) a 40-O-alkylated rapamycin.

29. A monoclonal antibody of claim 28 which recognizes an epitope on the FKBP-binding portion of a rapamycin.

30. A monoclonal antibody of claim 29, which recognizes an epitope on the effector portion of a rapamycin.

31. A monoclonal antibody of claim 28, obtained by:

a) reaction of a rapamycin having an activated coupling group with an immunogenic protein to produce an immunogenic conjugate;

b) administration of said immunogenic conjugate to an appropriate animal species to effect immunogenic challenge and recovery of antibody-producing cells sensitized to said conjugate;

c) immortalization of said antibody-producing cells; and

d) recovery of monoclonal antibody from a selected immortalized cell line thus established.

32. A monoclonal antibody of claim 28 wherein the rapamycin is rapamycin.

33. A monoclonal antibody of claim 28, wherein the 40-O-alkyl substituent is hydroxyalkyl, hydroxyalkoxyalkyl, acylaminoalkyl, or aminoalkyl.

34. A monoclonal antibody of claim 33 wherein the rapamycin is

i) 40-O-(2-hydroxyethyl)-rapamycin,

ii) 40-O-(3-hydroxypropyl)-rapamycin,

iii) 40-O-[2-(2-hydroxy)ethoxy]ethyl-rapamycin, or

iv) 40-O-(2-acetaminoethyl)-rapamycin).

35. A monoclonal antibody of claim 34, wherein the rapamycin is 40-O-(2-hydroxyethyl)-rapamycin.

36. A monoclonal antibody of claim 28 which distinguishes between (i) rapamycin and (ii) a 40-O-alkylated rapamycin.

37. A monoclonal antibody of claim 36 wherein the 40-O-alkyl substituent is hydroxyalkyl, hydroxyalkoxyalkyl, acylaminoalkyl, or aminoalkyl.

38. A hybridoma cell line which produces a monoclonal antibody of claim 28.

39. An immunoassay kit for measuring the blood level of a rapamycin, comprising a monoclonal antibody of claim 28.